

Delayed cyanide poisoning following acetonitrile ingestion

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Summary

Acetonitrile (methyl cyanide) is a common industrial organic solvent but is a rare cause of poisoning. We report the first recorded UK case. Acetonitrile is slowly converted to cyanide, resulting in delayed toxicity. We describe a case of deliberate self-poisoning by a 39-year-old woman resulting in cyanide poisoning 11 hours later which was successfully treated by repeated boluses of sodium nitrite and thiosulphate. The half-life of conversion of acetonitrile was 40 hours and harmful blood cyanide levels persisted for over 24 hours after ingestion. Departments treating or advising in cases of poisoning need to be aware of the delayed toxicity of acetonitrile. Monitoring in an intensive care unit of cases of acetonitrile poisoning should continue for 24–48 hours.

Keywords: cyanides, methyl cyanide, acetonitriles, poisoning

Acetonitrile is an industrial organic solvent and has been used in nail polish remover,^{1,2} but is a rare cause of poisoning. Characteristically, patients remain remarkably well until several hours after ingestion when biochemical and clinical features of cyanide poisoning occur. These are treatable and treated patients usually recover. A case is presented which was successfully treated and in whom plasma levels and pharmacokinetic measurements were made. To our knowledge this is the first reported UK case.

Case report

A 39-year-old woman was admitted after swallowing 25 g of acetonitrile (methyl cyanide) two hours previously in a suicide attempt. She vomited for half an hour following ingestion and was well apart from feeling mildly dizzy on admission. Physical examination was unremarkable. Full blood count, urea and electrolytes were normal. On oxygen her oxygen saturation (pulse oximetry) was 99% and hydrogen ion 36 mmol/l, pO₂ 33.2 kPa, pCO₂ 4.3 kPa, standard bicarbonate 24 mmol/l and base excess –1. Eleven hours following ingestion she became nauseated, confused and sweaty and tachycardic (140 beats/min). She developed Kussmaul respiration and became rapidly comatose. Blood gases on oxygen were hydrogen ion

101 mmol/l, pO₂ 22.5 kPa, pCO₂ 1.2 kPa, standard bicarbonate 1 and base excess –28. A diagnosis of acute cyanide poisoning was made and she was given 20 ml of 3% sodium nitrite and 200 ml of 25% sodium thiosulphate intravenously as bolus doses. Grand mal fits occurred, she was intubated and ventilated. Two hours later the methaemoglobin level was 15%, hydrogen ion 37 mmol/l, pO₂ 58.8 kPa, pCO₂ 3.1, standard bicarbonate 19 mmol/l and base excess –6. On day 2 she was stable but at 32 hours following ingestion became hypotensive and tachycardic with hydrogen ion 65 mmol/l, pO₂ 17.5 kPa, pCO₂ 3.8 kPa, standard bicarbonate 12 mmol/l and base excess –16. A further 30 ml of 3% sodium nitrite and three boluses of 20 ml of 25% sodium thiosulphate were administered. She continued to be acidotic with a base excess of –6 so a continuous infusion of 3% sodium nitrite at a rate of 2.5 ml/h was administered from day 4 to 5. She was extubated on day 6 but had to be reintubated due to the development of middle and bilateral basal pneumonia with the X-ray appearance of bilateral consolidation and right apical cavitation. Following successful treatment with intravenous cefotaxime and flucloxacillin she was finally discharged well 26 days following admission.

Blood levels of acetonitrile and cyanide are shown in the table. The half-life of acetonitrile was 36 h and of cyanide (excluding the initial level) 44 h.

Discussion

This case illustrates several important features of acetonitrile poisoning. Cyanide toxicity, characterised by vomiting and fitting, appears after an asymptomatic interval lasting several hours; the clinical state and acid–base balance promptly improves following treatment with sodium nitrite and sodium thiosulphate but then relapses following a further period of clinical stability.

Although acetonitrile is a widely used industrial solvent and has been available to

Table 1 Blood levels following admission

Times after admission (h)	Acetonitrile (mg/l)	Cyanide (mg/l)
5.5	640	0.85
15	470	1.7
19.5	360	1.36
57.5	140	0.37

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Features of cyanide poisoning⁹

- mild: dizziness, headaches, palpitations, anxiety, chest constriction, dyspnoea, confusion, vertigo
- severe: pulmonary oedema, metabolic acidosis, convulsions, respiratory arrest cardiovascular collapse

Box 1

Learning points

- acetonitrile is slowly converted to cyanide
- delayed cyanide poisoning occurs
- patients recover if correctly treated

Box 2

the public as nail polish remover,^{1,2} a Medline search of publications from 1991 to 95, including a bibliography of cases pre-1991, revealed only 12 reported cases of poisoning with four deaths.¹⁻⁹ Three of the four fatalities were discovered dead, but one child died without treatment because the substance was mis-identified as acetone and no antidote was given.² This is the first reported UK case.

The toxicity of acetonitrile is due to its oxidative metabolism by a hepatic cytochrome P450 related pathway to yield cyanide.² This process takes place over several hours resulting in the latent period between ingestion and poisoning. The half-life for acetonitrile conversion calculated from the four concentrations assuming a first-order process is 36 hours, which agrees closely with the 32 hours reported by Michaelis *et al.*⁶ As a result potentially lethal (greater than 1 mg/l) cyanide levels are found

over 24 hours after ingestion. We administered the standard treatment for cyanide poisoning with sodium nitrite and thiosulphate. Thiosulphate was successfully used in five of the reported cases. It acts by converting cyanide to thiocyanate which is then excreted in the urine. In two cases sodium nitrite was used. It acts by oxidising haemoglobin to methaemoglobin which has a higher affinity for cyanide than cytochrome oxidase.² Because of the continued generation of cyanide from acetonitrile, repeated doses of antidote may be needed. The cyanide half-life calculated from our figures (44 h) indicates that serious toxicity is likely for at least a day or two after ingestion. It may be wise to administer sodium thiosulphate and perhaps nitrite to all cases where acetonitrile has been ingested without waiting for acidosis to develop.

In the UK, dicobalt edetate is the standard textbook treatment for cyanide poisoning.⁹ It is not available in the US. It is more rapid in action than nitrite and thiosulphate and less toxic, provided the diagnosis is not in doubt. We are unaware of any cases where cobalt has been used for acetonitrile poisoning, however, so we used nitrite and thiosulphate based on the successful experience of others. Hyperbaric oxygen¹⁰ should not be required provided appropriate antidotes are given. The clinical features of vomiting, convulsions, coma and acidosis seem common to all cases reported. The combination of these features should prompt clinicians to think of cyanide poisoning. An oxygen saturation difference between pulse oximetry and that calculated from arterial blood gases, of greater than five² or direct blood cyanide or acetonitrile levels establishes the diagnosis.

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